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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/020,716	02/09/1998	RUDOLF JUNG	0815	3572

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EXAMINER

NELSON, AMY J

ART UNIT PAPER NUMBER

1638

36

DATE MAILED: 12/11/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/020,716

Applicant(s)

JUNG ET AL.

Examiner

Amy Nelson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 76-79,90-93 and 95-111 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 76-79,90-93 and 95-111 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 33,35 6) ☐ Other: _____

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DETAILED ACTION

Claim Rejections - 35 USC § 112

1. Claim 104 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "about 7 mole % to about 50 mole % lysine" and the phrase "about 6 mole % to about 40 mole % of a sulfur containing amino acid" does not appear to be supported by the instant specification. Applicant does not point to support for the phrase in the response filed 10/1/01. Applicant must point to support for the phrase or delete the new matter in response to this rejection.

2. Claims 76-79, and 90-93 remain rejected and new Claims 95-111 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reasons of record set forth in the Official action mailed 5/18/99 as applied to Claims 1-21, the Official action mailed 11/22/99 as applied to Claims 6, 7, 14-17, and 21-35, the Official action mailed 4/21/00 as applied to Claims 36-56, the Official action mailed

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8/9/00 as applied to Claims 57-74, and the Official action mailed 6/25/01 as applied to Claims 75-94. Applicant's arguments filed 10/1/01 have been fully considered but they are not persuasive.

Applicant asserts that pages 12-13 of the specification describe other suitable polypeptides than hordothionin. Applicant also asserts that description of ESA is in a pending application, now patented, and that the application has been amended to teach that information (response, p. 6). Examiner responds that although the specification refers to other wild type polypeptides, Applicant does not describe other modified nucleic acids nor plants comprising said nucleic acids that have increased lysine or sulfur-containing amino acids. Applicant does not state which pending application comprises a description of a modified ESA nucleic acid. Also, the instant application does not claim priority to that application. It is improper to incorporate essential material by reference. Hence, Applicant has not satisfied the written description requirement.

Applicant argues that references are incorporated into the specification, but Applicant does not provide the references, nor point to where they are cited in the specification. Applicant asserts that the genes can be modified to increase the level of lysine or sulfur-containing amino acids in the encoded protein. Further, Applicant asserts that other sulfur-rich proteins are known in the art, and Applicant cites several references (response, p. 7). Examiner responds that because Applicant did not point to specific locations in the specification and/or did not provide copies of the cited references, the references could not be considered. Applicant is invited to provide copies of references published prior to the filing date of the instant application that teach other

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nucleic acid molecules that could be used in the claimed method to increase lysine or sulfur-containing amino acids in plants.

Further, Applicant argues that Applicant has described numerous plant proteins other than hordothionin, and hence Applicant has described more than a single species of the claimed genus. Applicant points to pages 6-7 of the specification for a description of high lysine and high sulfur content proteins (response, p. 7-8). Examiner responds that the instant invention is directed to nucleic acid molecules and to transgenic plants, not to proteins, and hence Applicant need describe the nucleic acid molecules and transgenic plants with increased lysine or sulfur-containing amino acids. The cited pages 7-8 of the specification are a mere description of the concept, not of specific nucleic acid molecules that encode stable, active proteins with elevated levels of lysine or methionine-containing amino acids.

3. Claims 76-79, and 90-93 remain rejected and new Claims 95-111 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to transformed cereal plant seed having an elevated lysine, methionine and cysteine content (about 10% to about 35% by weight compared to untransformed cereal plant seed) comprising the modified hordothionin gene of SEQ ID NO:2 (HT12), vectors, plant cells and transformed plants comprising said modified hordothionin gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims. This rejection is repeated for the

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reasons of record set forth in the Official action mailed 5/18/99 as applied to Claims 1-21, the Official action mailed 11/22/99 as applied to Claims 6, 7, 14-17, and 21-35, the Official action mailed 4/21/00 as applied to Claims 36-56, the Official action mailed 8/9/00 as applied to Claims 57-74, and the Official action mailed 6/25/01 as applied to Claims 75-94. Applicant's arguments filed 10/1/01 have been fully considered but they are not persuasive.

Applicant argues that the amount of experimentation that must be considered is not the amount of experimentation required to practice the entire scope of the claim, but the amount of experimentation required to practice one embodiment of the claimed invention, and Applicant refers to an IgM antibody case (response, p. 9). Examiner responds that because Applicant has not cited the specific case law, it could not be considered. However, it is clear from *In re Wands* that Applicant need provide sufficient guidance to practice the claimed invention throughout the broad scope of the claims. Applicant has not provided such guidance in the instant application.

Applicant asserts that the present invention is enabled without more than routine experimentation by one of skill in the art. Applicant has taught both how to make and how to use the invention commensurate with the scope of the claims. Amino acid substitution is not the only suitable method to practice the claimed invention. Applicant can also select polypeptides that are naturally high in lysine or sulfur-containing amino acid content. The specification teaches promoters and other regulatory sequences, and Applicant has provided evidence of successful achievement of plants with increased amino acid content. Hence, the claimed invention is enabled (response, p. 10-11). Examiner responds that Applicant has not taught other nucleic

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acids than the nucleic acid sequence of SEQ ID NO:2 that can be used in the the claimed invention. Applicant has not taught other naturally occurring nucleic acid molecules that encode proteins with high lysine or sulfur-containing amino acids, and Applicant has not provided guidance for appropriate amino acid substitutions that do not affect protein stability or function, by mutation of wild types nucleic acid molecules. As admitted by Applicant "An important aspect of this approach is to be able to select a region of the protein that can be modified without affecting the overall structure, stability, function, and othe cellular and nutritional properties of the protein" (specification, p. 2, line 24 - p. 3, line 3). Hence, in the absence of appropriate guidance, one of skill in the art could not practice the claimed invention without undue trial and error experimentation.

Further, it is noted, with respect to newly amended claims 101-102, Applicant is not enabled for increased levels of lysine or sulfur-containing amino acids of about 10 times. With regard to Claim 104, Applicant is not enabled for levels of 50 mole % lysine or 40 mole % sulfur. Applicant provides no evidence of achieving such levels in the encoded polypeptides or in the transformed plants.

4. Claims 76-79, 90-93, and 95-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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At Claim 76, 77, 98, and 99, it is recommended that "the transformed cereal plant seed is from" be changed to -- transformed cereal plant is--.

At Claim 78, 95-97, 104-108, and 110, the phrase "plant derived polynucleotide" is indefinite. There are many different types of derivatives, and hence it is not known what is encompassed by "derived." It is recommended that the phrase be changed to --plant polynucleotide--.

At Claims 101 and 102, the phrase "about 10 times" is indefinite because it is not clear how the amino acid content is measured. Appropriate correction to state a standard measurement term, *e.g.* percent weight, is required.

Claim Rejections - 35 USC § 102

5. Claims 76-79, and 90-93 remain rejected and new Claims 95-111 are rejected under 35 U.S.C. 102(e) as being anticipated by Falco *et al.* (U.S. Patent 5,773,691). This rejection is repeated for the reasons of record as set forth in the last Official action mailed 6/25/01.

Applicant's arguments filed 10/1/01 have been fully considered but they are not persuasive.

Applicant asserts that the polynucleotides of Falco are not plant-derived, and therefore the claims of the instant invention are not anticipated by Falco (response, p. 13). Examiner responds that in view of the indefinite claim language "plant-derived polynucleotide" (which reads on essentially any polynucleotide, because any polynucleotide can be "derived" from a plant), the

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instantly claimed invention is still anticipated by the Falco reference. Further, it is noted that Falco does in fact teach plant polynucleotides (see, for example, Example 20).

Claim Rejections - 35 USC § 103

6. Claims 76-79, and 90-93 remain rejected, and new Claims 95-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao *et al.* (U.S. Patent 5,885,802) in view of Applicant's Admission. This rejection is repeated for the reasons of record as set forth in the last Official action mailed 6/25/01. Applicant's arguments filed 10/1/01 have been fully considered but they are not persuasive.

Applicant asserts that citing references that teach elements of the claims does not provide sufficient basis to conclude that the combination of elements would have been obvious. Constitutive expression and tissue-specific expression are entirely different and constitutive expression can have adverse affects on growth and development (response, p. 13-14). While the effects of constitutive expression and tissue-specific expression may be different, promoters serve a common function, namely to activate expression of an operably linked coding sequence. Hence, substitution of one promoter for another promoter is routine in the art. The fact that adverse affects are known to result from the use of a constitutive promoter would be a further motivating factor for substitution of a seed-specific or endosperm-specific promoter for the constitutive promoter of Rao.

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Applicant argues that Examiner provides no motivation to express the hordothionin gene in the endosperm. Applicant quotes Falco for teaching away from increasing lysine in the seed (response, p. 14). Examiner cannot consider the Falco teaching because Applicant has not cited a reference or a location in that reference for the quotation of Falco. The motivation provided by Examiner lies in the Rao reference itself. As Rao shows increases in amino acid composition in the seed (the major portion of which is the endosperm) with the constitutive promoter, one would have been motivated to substitute a seed-specific, or endosperm-specific promoter to further increase or to limit increases to the seed/endosperm tissue. The teachings of Rao are clearly directed to increasing amino acid composition in seeds, and Rao even teaches use of a seed-specific promoter (column 1, lines 35-36). Hence, it would have been an obvious modification to substitute an endosperm-specific promoter.

7. Claims 76-79, and 90-93 remain rejected and new Claims 95-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao *et al.* (U.S. Patent 5,990,389) in view of Applicant's Admission. This rejection is repeated for the reasons of record as set forth in the last Official action mailed 6/25/01. Applicant's arguments filed 10/1/01 have been fully considered but they are not persuasive.

Applicant asserts that citing references that teach elements of the claims does not provide sufficient basis to conclude that the combination of elements would have been obvious. Constitutive expression and tissue-specific expression are entirely different and constitutive

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expression can have adverse affects on growth and development (response, p. 15). While the effects of constitutive expression and tissue-specific expression may be different, promoters serve a common function, namely to activate expression of an operably linked coding sequence. Hence, substitution of one promoter for another promoter is routine in the art. The fact that adverse affects can result from use of a constitutive promoter would in fact be a further motivating factor for substitution of a seed-specific or endosperm-specific promoter for the constitutive promoter of Rao.

Applicant also argues that Examiner provides was no motivation to express the hordothionin gene in the endosperm. Applicant quotes Falco for teaching away from increasing lysine in the seed (response, p. 15). Examiner cannot consider the Falco teaching because Applicant has not cited a reference or a location in that reference for the quotation of Falco. The motivation provided by Examiner lies in the Rao reference itself. As Rao shows increases in amino acid composition in the seed (the major portion of which is the endosperm) with the constitutive promoter, one would have been motivated to substitute a seed-specific, or endosperm-specific promoter to further increase or to limit increases to the seed/endosperm tissue. The teachings of Rao are clearly directed to increasing amino acid composition in seeds. Hence, it would have been an obvious modification to substitute an endosperm-specific promoter.

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8. Claims 76-79, and 90-93 remain rejected and new Claims 95-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jaynes *et al.* (U.S. Patent 5,811,654) in view of Applicant's Admission. This rejection is repeated for the reasons of record as set forth in the Official action mailed 8/9/00 as applied to Claims 57-74, the Official action mailed 4/21/00 as applied to Claims 36-56, and the Official action mailed 6/25/01. Applicant's arguments filed 10/1/01 have been fully considered but they are not persuasive.

Applicant asserts that citing references that teach elements of the claims does not provide sufficient basis to conclude that the combination of elements would have been obvious. Constitutive expression and tissue-specific expression are entirely different and constitutive expression can have adverse affects on growth and development (response, p. 15). While the effects of constitutive expression and tissue-specific expression may be different, promoters serve a common function, namely to activate expression of an operably linked coding sequence. Hence, substitution of one promoter for another promoter is routine in the art. The fact that adverse affects can result from use of a constitutive promoter would in fact be a further motivating factor for substitution of a seed-specific or endosperm-specific promoter for the constitutive promoter of Jaynes.

Applicant also argues that Examiner provides was no motivation to express the hordothionin gene in the endosperm. Applicant quotes Falco for teaching away from increasing lysine in the seed (response, p. 15). Examiner cannot consider the Falco teaching because Applicant has not cited a reference or a location in that reference for the quotation of Falco. The

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motivation provided by Examiner lies in the Jaynes reference itself. As Jaynes shows increases in amino acid composition in the seed (the major portion of which is the endosperm), one would have been motivated to substitute a seed-specific, or endosperm-specific promoter to further increase or to limit increases to the seed/endosperm tissue. The teachings of Jaynes are clearly directed to increasing amino acid composition in seeds. Hence, it would have been an obvious modification to substitute an endosperm-specific promoter.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

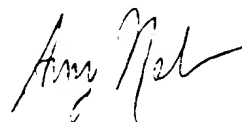
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy J. Nelson whose telephone number is (703) 306-3218. The examiner can normally be reached on Monday-Friday from 8:30 AM - 5:00 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Gwendolyn Payne, whose telephone number is (703) 305-2475.



AMY J. NELSON, PH.D
PRIMARY EXAMINER

Amy J. Nelson, Ph.D.

December 6, 2001